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Preoperative Anthropometric Dysmorphology in Metopic Synostosis

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ABSTRACT Anthropometric identification of dysmorphology in craniofacial anomalies, including the craniosynostoses, provides invaluable assistance in clinical diagnosis as well as offering a technique for interpreting possible deformities in skeletal remains. Premature closure of the metopic suture is a rare form of craniosynostosis, representing about 4% of clinically diagnosed synostoses. Accompanying this closure are defects of the head and face, particularly the upper face and orbits. To identify quantitatively the craniofacial dysmorphology associated with metopic synostosis, 50 patients with a diagnosis of primary (nonsyndromal) metopic synostosis were examined using a battery of 24 anthropometric measurements from which 11 proportion indices were calculated. The data were compared to sex- and age-matched normal standards and converted to standard (Z) scores before being analyzed using Student's *t*-test. The data indicate a complex pattern of dysmorphology arising from the synostosis which affects the upper face and orbits as well as the cranial vault. The entire fronto-orbito-zygomatic complex is narrowed, and vertex is reduced. There is compensatory sagittal and transverse growth of the posterior neurocranium and compensatory vertical and sagittal growth of the upper face. There are statistically significant differences in the pattern of dysmorphology between patients presenting prior to 6 months of age and those older but no significant differences between sexes. Am J Phys Anthropol 103:341–351, 1997.

Craniosynostosis, premature closure of one or more of the cranial sutures, has been recognized since the time of Hippocrates, who was one of the first to identify some of the cranial dysmorphology associated with abnormal suture fusion (Cohen, 1986). Numerous subsequent authors have identified other deformations associated with various synostoses. Otto (1830) described the compensatory growth of the skull that results from premature suture closure. This idea was adopted by Virchow (1851), who presented a system of classification which described the patterns of cranial deformation resulting from compensatory growth elsewhere in the skull.

Craniosynostosis can be inherited or sporadic. It can be isolated or syndromal. Estimates of the frequency of craniosynostosis range from about 0.4/1,000 (Hunter and Rudd, 1976) to 1.0/1,000 live births (Tessier, 1971). Higher estimates, such as those from skeletal collections (Bennett, 1967), probably reflect an ascertainment bias for more complete or unusual skulls (Cohen, 1986).

One of the rarer forms of craniosynostosis is premature fusion of the metopic suture.

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Normally, this suture begins closing at about 6 months of age. The chondroid tissue which is believed to be responsible for metopic suture closure has been identified microscopically as early as the twentieth week of gestational age, and suture closure has been noted histologically by 4 months of age (Manzanares et al., 1988). The suture is closed by the end of the first year of life (Krogman and Işcan, 1986) and is obliterated shortly thereafter.

Metopic synostosis generally accounts for 3–4% of all synostoses (Hunter and Rudd, 1976; Shillito and Matson, 1968), with a theoretical maximum of about 10% (Anderson and Geiger, 1965). This represents a prevalence between approximately 1/10,000 and 1/100,000 live births. The frontal keeling associated with metopic synostosis is the most obvious of the cranial deformities found in any of the nonsyndromal synostoses. Studies which have suggested that metopic synostosis involves over half of all craniosynostoses appear to reflect a diagnostic bias. Subjects were selected for study on the basis of visually apparent dysmorphology, with particular emphasis on ridging along suture lines, which is most obvious in metopic synostosis, less so in sagittal synostosis, and sporadic in other synostoses. This subgroup of clinical subjects subsequently was radiographed to confirm the diagnoses. The result was a reported incidence of metopic synostosis of 56% of all the patients submitted to x-ray (Shuper et al., 1985).

Clinical studies indicate a predominance of males over females with metopic synostosis. Published sex ratios range from 2:1 (DiRocco et al., 1989; Friede et al., 1990; Genitori et al., 1991) to as high as 6.5:1 (Dhellemmes et al., 1986).

Clinically, patients with metopic synostosis have been recognized as having several deformities of the fronto-orbital region (Table 1). These include a prominent, prow-shaped forehead with a ridge, or keel, along the metopic suture and a trigonocephalic skull shape. Orbital findings involve orbital hypotelorism, or a reduced transverse distance between the orbits, as well as an upslant to the eye fissures and deficient lateral orbital rims (Delashaw et al., 1989, 1991; Friede et al., 1990; Graham, 1988; Persing et al., 1989).

TABLE 1. Clinical features of metopic synostosis

Narrow, prow-shaped forehead
Metopic suture ridge
Trigonocephaly
Hypotelorism
Upslanted palpebral fissures
Deficient lateral orbital rims

It has been suggested by Delashaw et al. (1989, 1991) that trigonocephaly is a result of compensatory growth of the sagittal and coronal sutures. In particular, it has been suggested that, while growth remains symmetrical on both sides of the sagittal suture, it is asymmetrical at the coronal suture. Growth is said to be greater along the parietal edge of the coronal suture than along the frontal edge because of the effect of the synostosis. The result is increased posterolateral growth of the skull which produces a pear-shaped skull (Delashaw et al., 1989, 1991).

The etiology of metopic synostosis is heterogeneous. It has been associated with several syndromes as well as a number of chromosomal anomalies. Clinical studies indicate the presence of associated anomalies in about 17–25% of all patients (Andersson and Gomes, 1968; Bertelsen, 1958; Shillito and Matson, 1968). Despite this, most cases appear to be sporadic, though the occurrence of spontaneous mutations remains a possibility (Cohen, 1986). Instances of metopic synostosis resulting from fetal head constraint also have been reported (Graham, 1988; Graham and Smith, 1980).

Skeletal examples of premature metopic synostosis are extremely rare, whether from archaeological or medical collections. Bolk (1915), for example, did not find any instances in his study of European skulls. Bennett (1967) did not record any examples in his analysis of over 1,000 crania in the collections of the Arizona State Museum or from reports from other prehistoric Southwest sites. The fragility of infant skulls decreases the likelihood of their preservation in archeological sites and, subsequently, the ability to identify such a rare phenomenon in what are usually very fragmentary remains.

In older individuals who might have had premature closure of the metopic suture as

infants and survived to adolescence or adulthood, diagnosis might be made difficult by continuing cranial growth and remodeling and by the lack of adequate craniometric data and analysis from the relevant areas of the fronto-orbital complex. For example, recently it has been suggested that a skull in the Salzburg Museum, identified as belonging to Wolfgang Amadeus Mozart, shows evidence of premature closure of the metopic suture, based on certain peculiarities of the supraorbital rim and a limited set of craniometric measurements (Puech et al., 1989a,b). Other researchers, examining the same skull, find no such evidence and offer other diagnoses (Czorny and Ricbourg, 1992; Hauser and Kritscher, 1994).

Clinically, there are very few quantitative data describing the dysmorphology of patients with metopic synostosis. The most extensive attempt is a report of 14 horizontal measurements taken from three CT scan slices of a sample of ten clinical subjects (Posnick et al., 1994). The anthropometric protocol used at the Columbia Craniofacial Center at Medical City Dallas Hospital provides a much larger battery of quantitative traits, craniofacial measurements, and proportions from which to evaluate the patterns of dysmorphology in all three dimensions in a wide variety of craniofacial anomalies, including metopic synostosis.

To test the hypothesis that premature closure of cranial vault sutures causes compensatory growth throughout the head and face that results in widespread dysmorphology, we examined anthropometric data from a group of patients with isolated (i.e., nonsyndromal) metopic synostosis from the Columbia Craniofacial Center at Medical City Dallas Hospital to identify the resulting patterns of dysmorphology, including any potential age- or sex-related differences in these patterns. The clinical findings were compared to published data from the skull of Mozart to examine the hypothesis that he exhibited premature metopic suture closure.

MATERIALS AND METHODS

The sample consisted of 50 preoperative patients (12 females, 38 males) with a radiologically confirmed diagnosis of isolated metopic synostosis (Fig. 1), ranging in age from 2–69 months ($\bar{x}$ = 17.5 months). The patients were assessed using a set of 24 anthropometric measurements of the head and face derived from a much larger assessment battery, which has been presented previously (Kolar et al., 1987; Kolar and Salter, 1996) (Fig. 2). From these, 11 proportion indices were calculated to evaluate craniofacial shape (Csima and Szathmáry, 1987; Farkas and Munro, 1987). All measurements were taken by one of the authors (J.C.K.), who has been conducting clinical studies in craniofacial anthropometry since 1983.

The individual measurements and proportions for each patient were compared to age- and sex-matched normal standards (Hajniš, 1974, as adjusted by Csima and Szathmáry, 1987; Dekaban, 1977) and converted to standard ($Z = x - \bar{x}/s.d.$) scores to adjust for age and sex. The standardized data for each variable were pooled, mean Z scores and standard deviations were calculated for each variable, and the results were analyzed using Student's *t*-test (Kolar et al., 1987). The entire sample was compared to normal standards using a single-sample *t*-test (Campbell, 1989) to test the null hypothesis ($\bar{x}Z_x = 0$). The standardized data were then separated into two broad age groups: patients less than 6 months old (n = 17; 3 females, 14 males), and those 6 months and older (n = 33; 9 females, 24 males). The younger group included all those patients who would normally be expected to have an open metopic suture, while the older subjects covered the period of normal suture closure. Each subsample was compared to the normal standards separately using a single-sample *t*-test before the two groups were compared using paired *t*-tests to test the null hypothesis that there is no significant difference in craniofacial dysmorphology between early- and late-appearing patients with metopic synostosis ($\bar{x}Z_a = \bar{x}Z_b$). Finally, the data were pooled by sex and analyzed first separately with single-sample *t*-tests to determine any significant differences from normal standards before being compared using paired *t*-tests to determine if there were any sex-related differences in craniofacial dysmorphology in these patients ($\bar{x}Z_m = \bar{x}Z_f$).

Fig. 1. Frontal (**left**) and submental vertex (**right**) views of 5-month-old male with metopic synostosis, showing typical frontal keel and trigonocephalic head shape with flattened superior orbital rims and narrow interorbital distance.

Because the possibility of significant results occurring by chance (type I error) increases with the number of variables tested, the level of significance was recalculated using Bonferroni's correction (α/m), where α is the initial probability (.05) and m is the number of tests (35) (Manly, 1992). This yielded an adjusted probability of $P <$ .0014 (rounded to $P <$ .001), which produces a cumulative confidence interval of .95 $[(1 - \alpha/m)^m]$ for the total set of variables. However, while Bonferroni's correction reduces the possibility of type I statistical error, it simultaneously increases the possibility of type II error, resulting in acceptance of the null hypothesis when it is false, thereby overlooking clinically important findings. To avoid this error, all significant results are shown, with those significant at the $P <$ .001 level noted with an asterisk (*).

RESULTS

The results of the Z-score analysis are presented in Tables 2–4. Table 2 gives the findings for the combined sample of 50 patients. Table 3 presents the results separately for the two age groups and compares the subsamples to each other. The data in Table 4 are sorted by sex, with comparisons to the normal standards and to each other. In each table, the data are presented by anatomical region, beginning with the head, with the measurements listed before the proportions in each region.

Of the 35 variables tested, 25 (18 of 24 measurements, 7 of 11 proportions) were significant for the total sample of patients (n = 50) using a single-sample *t*-test. When the sample is divided into two age-related subsets (age <6 months, age ≥6 months), 30 of 35 variables (20 measurements, 10 propor-

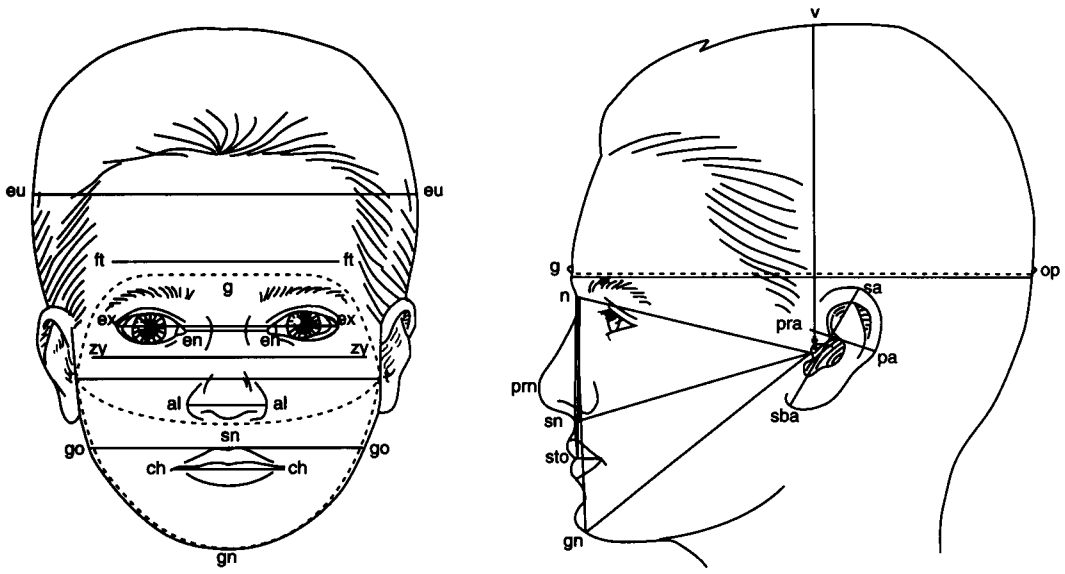

Fig. 2. Schematic drawing of basic anthropometric measurement battery (see Tables 2–4).

tions) are significant in the younger group, and 22 (15 measurements, 7 proportions) are significant in the older group. When the Z-score data from the two subsets are compared using two-sample *t*-tests, 23 of the 35 variables (17 measurements, 6 proportions) differ significantly. Finally, the male subjects exhibit significant findings in 26 of 35 variables (19 measurements, 7 proportions), while females show 17 significant variables (10 measurements, 7 proportions). There are no significant differences between sexes when Bonferroni's correction is applied.

DISCUSSION

The anthropometric data indicate a much more extensive series of craniofacial anomalies associated with metopic synostosis than has been reported previously in the clinical literature. Our results confirm the characteristic narrow forehead, trigonocephalic skull shape, and orbital defects that result from deficient fronto-orbital growth, including orbital hypotelorism and deficient lateral orbital rims (see Table 1). Patients exhibit general craniofacial enlargement with growth restrictions in the fronto-orbito-zygomatic region, compensatory growth elsewhere in the skull, and restriction in vertical cranial growth. Increases in cranial length (g-op) and biparietal width (eu-eu) are consistent with previous reports of compensatory postero-lateral skull growth (Delashaw et al., 1989, 1991) in metopic synostosis, although the cephalic index (eu-eu/g-op) remains within normal limits. The increased head circumference reflects the increased head size, but the vertical reduction (v-po) may at least partially offset this. The cranial base, as indicated by normal width (t-t) and normal ear size and shape (pra-pa/sa-sba), appears uninvolved. There is a general narrowing of the entire fronto-orbital area to the level of the zygomatic arches (zy-zy). This is most apparent in the proportions between the minimum frontal breadth (ft-ft) and the other transverse dimensions of the head and face. The combination of narrowed forehead and increased biparietal width produces a markedly reduced frontoparietal index (ft-ft/eu-eu) reflecting the characteristic trigonocephaly of metopic synostosis. The frontobasal index (ft-ft/t-t) also is dysmorphic but not to the extent of the frontoparietal index because of the normal cranial base width. On the other hand, the frontozygomatic index (ft-ft/zy-zy) is average, despite the large variance, because of the effect of anterior cranial narrowing on face width.

TABLE 2. Standardized (Z score) anthropometric findings in a combined sample of 50 preoperative patients with metopic synostosis[1]

	N	Mean	SD	t	*P*
Cranial dimensions					
eu-eu	50	0.505	1.183	3.019	<.01
ft-ft	50	−0.478	1.012	3.340	<.01
t-t	50	0.191	0.978	1.381	
g-op	50	0.439	0.935	3.320	<.01
v-po	46	−1.712	1.201	9.668	<.001*
Circumference	49	1.035	1.493	4.853	<.001*
Cranial proportions					
eu-eu/g-op	50	0.264	1.088	1.716	
ft-ft/eu-eu	50	−1.078	1.550	4.918	<.001*
ft-ft/t-t	50	−0.734	1.401	3.705	<.001*
ft-ft/zy-zy	50	0.005	2.706	0.013	
Facial dimensions					
zy-zy	50	−0.103	1.259	0.578	
go-go	50	0.579	1.127	3.633	<.001*
n-gn	49	0.483	1.121	3.016	<.01
n-sto	49	0.690	1.233	3.917	<.001*
n-t 1	46	1.087	0.842	8.756	<.001*
sn-t 1	46	1.681	1.040	10.963	<.001*
gn-t 1	46	1.449	0.936	10.500	<.001*
t-g-t	47	0.051	0.878	0.398	
t-sn-t	47	1.173	1.147	7.011	<.001*
t-gn-t	47	1.789	1.113	11.020	<.001*
Facial proportions					
n-gn/zy-zy	49	0.810	1.155	4.909	<.001*
n-sto/zy-zy	49	1.142	1.196	6.684	<.001*
Orbital dimensions					
en-en	50	−1.752	0.824	15.035	<.001*
ex-ex	50	−0.910	0.911	7.063	<.001*
Orbital proportions					
en-en/ex-ex	50	−1.666	1.165	10.112	<.001*
Nasal dimensions					
al-al	50	0.128	0.927	0.976	
n-sn	50	0.951	1.302	5.165	<.001*
sn-prn	49	0.438	0.964	3.180	<.01
Nasal proportions					
al-al/n-sn	50	−1.153	1.429	5.705	<.001*
al-al/zy-zy	50	0.270	0.998	1.913	
Orolabial dimensions					
ch-ch	46	−0.733	0.754	6.593	<.001*
Orolabial proportions					
ch-ch/zy-zy	46	−0.961	0.904	7.210	<.001*
Ear dimensions					
pra-pa 1	45	0.115	0.840	0.918	
sa-sba 1	45	−0.339	1.197	1.900	
Ear proportions					
pra-pa/sa-sba	45	0.068	1.276	0.357	

[1] Abbreviations: Landmarks. al = alare; ch = cheilion; en = endocanthion; eu = euryon; ex = exocanthion; ft = frontale; g = glabella; gn = gnathion; go = gonion; n = nasion; op = opisthocranion; pa = postaurale; po = porion; pra = preaurale; prn = pronasale; sa = superaurale; sba = subaurale; sn = subnasale; sto = stomion; t = tragion; v = vertex; zy = zygion. Measurements. al-al = soft nose width; ch-ch = labial fissure width; en-en = intercanthal width; eu-eu = maximum cranial breadth; ex-ex = biocular breadth; ft-ft = minimum frontal breadth; g-op = maximum cranial length; gn-t = mandibular depth; go-go = mandible (bigonial) width; n-gn = physiognomical face height; n-sn = nose height; n-sto = upper face height; n-t = upper face depth; pra-pa = ear width; sa-sba = ear length; sn-prn = nasal tip protrusion; sn-t = maxillary depth; t-g-t = supraorbital arc; t-gn-t = mandibular arc; t-sn-t = maxillary arc; t-t = cranial base width; v-po = auricular head height; zy-zy = maximum facial (bizygomatic) width.
* Significant when adjusted for Bonferroni's inequality (Manly, 1992).

One axis of cranial growth is neglected in the anthropological and clinical literature: the vertical dimension. The skull tends to be analyzed as if it were a two-dimensional object, with breadth and length but not height. Certainly the references on growth restriction and compensation show this tendency (Virchow, 1851; Graham, 1988; Delashaw et al., 1989, 1991). However, our data indicate that vertical growth restriction, as expressed in reduced auricular head height (v-po), is one of the most significant components of the overall anterior craniofacial growth anomalies in metopic synostosis.

TABLE 3. Comparison of standardized (Z score) anthropometric findings in metopic synostosis by age[1]

	<6 months					6+ months					Comparison		
	N	Mean	SD	t	*P*	N	Mean	SD	t	*P*	N	t	*P*
Cranial dimensions													
eu-eu	17	1.321	1.032	5.278	<.001*	33	0.085	1.037	0.471		50	4.000	<.001*
ft-ft	17	−0.417	1.180	1.457		33	−0.510	0.933	3.140	<.01	50	0.305	
t-t	11	0.961	0.602	6.582	<.001*	33	−0.206	0.899	1.316		50	4.822	<.001*
g-op	17	0.740	0.585	5.216	<.001*	33	0.283	1.045	1.556		50	1.668	
v-po	15	−1.317	1.007	5.065	<.001*	31	−1.903	1.255	8.443	<.001*	46	1.546	
Circumference	17	2.008	1.435	5.769	<.001*	32	0.519	1.264	2.323	<.05	49	3.650	<.001*
Cranial proportions													
eu-eu/g-op	17	0.874	1.218	2.959	<.01	33	−0.050	0.878	0.327		50	3.080	<.01
ft-ft/eu-eu	17	−2.094	2.079	4.153	<.001*	33	−0.554	0.829	3.839	<.001*	50	3.747	<.001*
ft-ft/t-t	17	−1.602	1.792	3.686	<.01	33	−0.287	0.889	1.855		50	3.488	<.01
ft-ft/zy-zy	17	−1.682	3.204	2.281	<.05	33	0.874	1.945	2.581	<.02	50	3.511	<.001*
Facial dimensions													
zy-zy	17	1.067	1.023	4.300	<.001*	33	−0.706	0.896	4.526	<.001*	50	6.310	<.001*
go-go	17	1.823	0.708	10.616	<.001*	33	−0.062	0.671	0.531		50	9.240	<.001*
n-gn	17	1.253	1.021	5.060	<.001*	32	0.074	0.953	0.439		49	3.943	<.001*
n-sto	17	1.261	0.753	6.905	<.001*	32	0.388	1.338	1.640		49	2.439	<.02
n-t 1	14	1.465	0.660	8.305	<.001*	32	0.921	0.868	6.02	<.001*	46	2.053	<.05
sn-t 1	14	2.414	0.700	12.903	<.001*	32	1.360	1.008	7.632	<.001*	46	3.479	<.01
gn-t 1	14	2.235	0.663	12.613	<.001*	32	1.106	0.829	7.547	<.001*	46	4.410	<.001*
t-g-t	14	0.736	0.700	3.934	<.01	33	−0.240	0.785	1.756		47	4.540	<.001*
t-sn-t	14	2.344	0.797	11.004	<.001*	33	0.675	0.882	4.396	<.001*	47	5.961	<.001*
t-gn-t	14	2.943	0.900	12.235	<.001*	33	1.300	0.789	9.465	<.001*	47	6.108	<.001*
Facial proportions													
n-gn/zy-zy	17	0.823	1.215	2.793	<.02	32	0.796	1.151	3.912	<.001*	49	0.075	
n-sto/zy-zy	17	1.239	1.037	4.926	<.001*	32	1.090	1.286	4.795	<.001*	49	0.404	
Orbital dimensions													
en-en	17	−1.752	0.728	9.923	<.001*	33	−1.752	0.880	11.437	<.001*	50	0.000	
ex-ex	17	−0.480	0.679	2.915	<.02	33	−1.132	0.944	6.889	<.001*	50	2.527	<.02
Orbital proportions													
en-en/ex-ex	17	−2.204	1.148	7.916	<.001*	33	−1.388	1.088	7.329	<.001*	50	2.465	<.02
Nasal dimensions													
al-al	17	0.928	0.700	5.466	<.001*	33	−0.285	0.746	2.195	<.05	50	5.339	<.001*
n-sn	17	1.487	1.045	4.867	<.001*	33	0.710	1.330	3.067	<.01	50	2.094	<.05
sn-prn	17	0.603	0.837	2.970	<.01	32	0.350	1.027	1.928		49	0.855	
Nasal proportions													
al-al/n-sn	17	−1.548	1.611	3.962	<.01	33	−0.950	1.305	4.182	<.001*	50	1.417	
al-al/zy-zy	17	0.179	0.889	0.830		33	0.316	1.060	1.713		50	0.457	
Orolabial dimensions													
ch-ch	14	−0.211	0.707	1.117		32	−0.961	0.662	8.212	<.001*	46	3.394	<.01
Orolabial proportions													
ch-ch/zy-zy	14	−0.940	0.744	4.727	<.001*	32	−0.954	0.981	5.501	<.001*	46	0.047	
Ear dimensions													
pra-pa 1	15	0.211	0.707	1.186		30	0.066	0.913	0.396		45	0.531	
sa-sba 1	15	0.111	0.773	0.556		30	−0.563	1.314	2.347	<.05	45	1.793	
Ear proportions													
pra-pa/sa-sba	15	−0.652	1.028	2.456	<.05	30	0.427	1.249	1.873		45	2.817	<.01

[1] Abbreviations: Landmarks. al = alare; ch = cheilion; en = endocanthion; eu = euryon; ex = exocanthion; ft = frontale; g = glabella; gn = gnathion; go = gonion; n = nasion; op = opisthocranion; pa = postaurale; po = porion; pra = preaurale; prn = pronasale; sa = superaurale; sba = subaurale; sn = subnasale; sto = stomion; t = tragion; v = vertex; zy = zygion. Measurements. al-al = soft nose width; ch-ch = labial fissure width; en-en = intercanthal width; eu-eu = maximum cranial breadth; ex-ex = biocular breadth; ft-ft = minimum frontal breadth; g-op = maximum cranial length; gn-t = mandibular depth; go-go = mandible (bigonial) width; n-gn = physiognomical face height; n-sn = nose height; n-sto = upper face height; n-t = upper face depth; pra-pa = ear width; sa-sba = ear length; sn-prn = nasal tip protrusion; sn-t = maxillary depth; t-g-t = supraorbital arc; t-gn-t = mandibular arc; t-sn-t = maxillary arc; t-t = cranial base width; v-po = auricular head height; zy-zy = maximum facial (bizygomatic) width.
* Significant when adjusted for Bonferroni's inequality (Manly, 1992).

The growth disturbances produced by metopic synostosis also affect the other growth patterns of the face and its individual components. The face is generally enlarged in all directions, with the exceptions of face width, indicated above, and the length of the supraorbital arc. These can be explained by the growth restrictions related to the closure of the metopic suture, whether or not this is the result of fetal head constraint.

The elongation and increased depth of the upper face, which consists of the orbits and maxilla, seems to reflect redirected growth resulting from the constriction of the fronto-

TABLE 4. Comparison of standardized (Z score) anthropometric findings in metopic synostosis by sex[1]

	Females					Males					Comparison		
	N	Mean	SD	t	*P*	N	Mean	SD	t	*P*	N	t	*P*
Cranial dimensions													
eu-eu	12	0.703	1.531	1.591		38	0.441	1.067	2.548	<.02	50	0.649	
ft-ft	12	−0.737	0.627	4.072	<.01	38	−0.397	1.101	2.223	<.05	50	0.997	
t-t	12	−0.004	1.162	0.012		38	0.253	0.922	1.692		50	0.772	
g-op	12	0.229	1.024	1.011		38	0.482	0.915	3.247	<.01	50	0.575	
v-po	12	−1.403	0.819	5.934	<.001*	34	−1.821	1.302	8.155	<.001*	46	1.020	
Circumference	12	1.242	2.049	2.100		37	0.968	1.293	4.554	<.001*	49	0.534	
Cranial proportions													
eu-eu/g-op	12	0.321	0.922	1.206		38	0.247	1.146	1.329		50	0.199	
ft-ft/eu-eu	12	−1.549	1.374	3.905	<.01	38	−0.924	1.593	3.576	<.01	50	1.197	
ft-ft/t-t	12	−0.829	1.265	2.270	<.05	38	−0.704	1.455	2.983	<.01	50	0.262	
ft-ft/zy-zy	12	−0.053	2.164	0.085		38	0.024	2.881	0.051		50	0.084	
Facial dimensions													
zy-zy	12	−0.425	1.263	1.166		38	−0.002	1.258	0.010		50	1.000	
go-go	12	0.359	1.112	1.118		38	0.651	1.141	3.517	<.01	50	0.762	
n-gn	11	0.816	1.622	1.743		38	0.387	0.936	2.549	<.02	49	1.089	
n-sto	11	0.603	1.428	1.401		38	0.715	1.191	3.701	<.001*	49	0.257	
n-t 1	10	0.732	0.984	2.352	<.05	36	1.185	0.785	9.057	<.001*	46	1.490	
sn-t 1	10	1.284	1.327	3.060	<.02	36	1.791	0.937	11.469	<.001*	46	1.341	
gn-t 1	10	1.060	1.121	2.990	<.02	36	1.559	0.863	10.839	<.001*	46	1.476	
t-g-t	11	−0.100	0.949	0.349		36	0.062	0.867	0.429		47	0.519	
t-sn-t	11	1.034	1.436	2.388	<.05	36	1.215	1.065	6.845	<.001*	47	0.443	
t-gn-t	11	1.737	1.136	5.071	<.001*	36	1.805	1.122	9.739	<.001*	47	0.172	
Facial proportions													
n-gn/zy-zy	11	1.438	1.384	3.446	<.01	38	0.628	1.031	3.755	<.001*	49	2.132	<.05
n-sto/zy-zy	11	1.393	1.524	3.032	<.02	38	1.069	1.097	6.007	<.001*	49	0.792	
Orbital dimensions													
en-en	12	−2.025	0.812	8.639	<.001*	38	−1.666	0.819	12.540	<.001*	50	1.301	
ex-ex	12	−0.900	0.999	3.121	<.01	38	−0.914	0.896	6.288	<.001*	50	0.045	
Orbital proportions													
en-en/ex-ex	12	−2.075	0.963	7.464	<.001*	38	−1.536	1.204	7.864	<.001*	50	1.386	
Nasal dimensions													
al-al	12	0.088	0.966	0.316		38	0.140	0.928	0.930		50	0.164	
n-sn	12	0.632	1.311	1.670		38	1.052	1.300	4.988	<.001*	50	0.955	
sn-prn	12	0.078	0.884	0.306		37	0.555	0.971	3.477	<.01	49	1.481	
Nasal proportions													
al-al/n-sn	12	−0.979	1.263	2.685	<.05	38	−1.210	1.493	4.996	<.001*	50	0.486	
al-al/zy-zy	12	0.194	0.722	0.931		38	0.293	1.078	1.675		50	0.292	
Orolabial dimensions													
ch-ch	12	−1.064	0.745	4.434	<.001*	34	−0.616	0.732	4.907	<.001*	46	1.771	
Orolabial proportions													
ch-ch/zy-zy	12	−1.101	0.911	4.187	<.01	34	−0.890	0.920	5.641	<.001*	46	0.670	
Ear dimensions													
pra-pa 1	11	−0.424	0.725	1.940		34	0.289	0.808	2.086	<.05	45	2.546	<.02
sa-sba 1	11	−0.055	0.653	0.279		34	−0.430	1.321	1.898		45	0.887	
Ear proportions													
pra-pa/sa-sba	11	−0.517	1.010	1.698		34	0.325	1.296	1.462		45	1.927	

[1] Abbreviations: Landmarks. al = alare; ch = cheilion; en = endocanthion; eu = euryon; ex = exocanthion; ft = frontale; g = glabella; gn = gnathion; go = gonion; n = nasion; op = opisthocranion; pa = postaurale; po = porion; pra = preaurale; prn = pronasale; sa = superaurale; sba = subaurale; sn = subnasale; sto = stomion; t = tragion; v = vertex; zy = zygion. Measurements. al-al = soft nose width; ch-ch = labial fissure width; en-en = intercanthal width; eu-eu = maximum cranial breadth; ex-ex = biocular breadth; ft-ft = minimum frontal breadth; g-op = maximum cranial length; gn-t = mandibular depth; go-go = mandible (bigonial) width; n-gn = physiognomical face height; n-sn = nose height; n-sto = upper face height; n-t = upper face depth; pra-pa = ear width; sa-sba = ear length; sn-prn = nasal tip protrusion; sn-t = maxillary depth; t-g-t = supraorbital arc; t-gn-t = mandibular arc; t-sn-t = maxillary arc; t-t = cranial base width; v-po = auricular head height; zy-zy = maximum facial (bizygomatic) width.
* Significant when adjusted for Bonferroni's inequality (Manly, 1992).

orbital area, in the same manner as the compensatory growth of the skull. The sagittal increase is greatest in the maxilla (sn-t l) due to the combined effects of increased anterior and vertical growth of the upper face, while upper face depth (n-t l) appears affected only by the anterior increase. The mandible is increased in width (go-go), depth (gn-t l), and contour (t-gn-t), with the sagittal increase intermediate between the upper face and maxilla.

The increased sagittal depth of the face, which is greater than the vertical increase, may be related to the inclination of the middle cranial fossa, which has been suggested as a causative factor in facial growth.

A more anteriorly inclined fossa produces a longer, more protruded upper face and maxilla and posteroinferior rotation of the mandible. In addition, it is associated with elongation of the cranial vault, which is characteristic of our metopic synsotosis patients (Enlow, 1989). An anterior orientation of the fossa will produce a flatter cranial base angle. This in turn will change the Frankfort line by elevating porion relative to the inferior orbital rim, change the location of the cranial vertex, and affect the auricular head height (v-po). This may account for the reduction in this dimension in our patients.

The most severe defects are found in the orbits. With the lower forehead and upper face, this region is compressed, with both intercanthal (en-en) and biocular (ex-ex) widths reduced. The orbits are hypoteloric, with a below average to narrow intercanthal width in all 50 patients. The intercanthal width is significantly more reduced than the biocular width ($t = 4.811$; $P < .001$), resulting in a relatively hypoteloric intercanthal index (en-en/ex-ex). This reflects the midline nature of the defect, with the most severe reduction nearest the obliterated or agenetic suture and lesser defects lateral to the area of the primary anomaly. Published measurements of interorbital distance from CT slices of a small sample ($n = 10$) of these patients indicate slightly greater skeletal involvement (Fearon et al., 1996).

Defects in the remaining facial regions are limited. Like the upper face, the height of the nose (n-sn) is increased. The resulting nasal index (al-al/n-sn) is relatively leptorrhine, although the soft nose (al-al) is actually relatively wide for the face. The labial fissure (ch-ch) is significantly reduced, and the ears are normal in size and shape.

Comparison of the two broad age categories, those patients under 6 months of age and those 6 months and older, indicates many consistencies in the findings but also some significant differences, primarily in the neurocranium and the overall facial framework (Table 3). With one exception, the heads of the younger patients are larger and more dysmorphic. Of particular importance are the increased biparietal (eu-eu) and cranial base (t-t) widths. Both are significantly widened in the younger group and normal in the older. The auricular head height (v-po) is reduced in both groups but is lower in the older patients, though the difference is not significant. The net effect of these differences is a brachycephalic head shape in the younger group, which is significantly more trigonocephalic, as reflected in the smaller frontoparietal index.

The facial dimensions of the younger patients all are large and generally significantly larger than the older subjects. The most striking difference between the two groups is in the width of the face. Both bizygomatic (zy-zy) and bigonial (go-go) breadths are abnormally wide in the younger group but not the older. Bizygomatic breadth is actually abnormally narrow in the older group and relatively narrower than the forehead, as reflected in the significant change in the frontozygomatic index (ft-ft/zy-zy). The facial (n-gn/zy-zy) and upper facial (n-sto/zy-zy) indices both indicate relative elongation of the face in both age groups.

The orbits show a mixture of cranial and facial changes between the two age groups. The intercanthal width shows no difference between groups, similar to the finding in the minimum frontal breadth. The biocular width is narrower in the older group, though the difference is not as marked as that seen in the bizygomatic breadth. The result is a significantly increased, though still hypoteloric, intercanthal index in the patients 6 months of age and older.

The nasal findings reflect the overall facial pattern. The nose is large and relatively leptorrhine, more so in the younger age group. The labial fissure is relatively narrow for the face, with the greater reduction width in the older group proportionate to the overall narrowing of the face. Finally, the ears are absolutely and relatively shorter in the older group, though this may represent an instance of type I error.

The cause of these age-related differences is uncertain. Because this is a clinical sample, the patients almost invariably present for their initial examination at the time of surgery. As a result, individual growth patterns cannot be determined. The older group may represent the milder end of the spectrum of dysmorphology at birth in whom growth deficiencies produce clinical symp-

toms at a later age, or their anomalies may have been consistent since birth but not recognized as clinically significant until later, or they may represent improved postnatal growth which has not corrected the initial defects. The last, by parental report, is the least likely scenario.

Bonferroni's correction has a greater effect on the results for the age-sorted subsamples than was apparent in the total sample. Much of the difference is due to the greater values of t required to achieve statistical significance in the smaller samples, especially in the younger age group. However, with the possible exception of the ears findings mentioned above, the data appear consistent despite some lower levels of probability.

Our data indicate a sex ratio slightly more than 3:1, males over females (38 males, 12 females), within the range of other reports indicating male predominance in metopic synostosis (Dhellemmes et al., 1986; DiRocco et al., 1989; Friede et al., 1990; Genitori et al., 1991). However, the anthropometric data show no significant differences between males and females in either craniofacial dimensions or proportions when Bonferroni's correction is applied. The reduced probabilities in the female subsample reflect its much smaller sample size. If sex is not a significant factor in the patterns of dysmorphology we have recorded in patients with metopic synostosis, what can explain the higher incidence of affected males?

The data are consistent with published reports emphasizing fetal head size as a determining factor in metopic synostosis (Graham et al., 1979; Graham and Smith, 1980; Graham, 1983). Both sexes show the general craniofacial enlargement, except for the anterior cranio-orbito-zygomatic region, typical of the entire group. The anterior cranium and adjacent areas of the upper face are narrowed, while the posterior cranium and lower face display compensatory growth. Male cranial growth is reported to be greater than female in the last trimester, resulting in a higher incidence of craniosynostosis (Graham et al., 1979; Graham and Smith, 1980; Graham, 1983). Since our metopic synostosis patients show the same sex ratio that has been reported for sagittal synostosis, and both reflect synostosis of midline cranial sutures, they may result from similar patterns of constraint, with differences in intrauterine head position producing different areas of localized constraint affecting different portions of these midline sutures. In particular, there is an association between large fetal head size and face presentation, which occurs in approximately 1:1,200 live births (Cunningham et al., 1993). Such presentation could produce the constraint necessary to cause metopic synostosis. This possibility also is suggested by the fact that the youngest females ($n = 3$) in our sample show even greater biparietal and cranial base widths, maximum cranial length, and head circumference than do the males of the same age, indicating large-headed females exhibit the same pattern of dysmorphology as males.

To examine the application of clinical anthropometric findings to skeletal remains, we compared our findings for metopic synostosis patients to published craniometric data for Mozart's skull (Puech et al., 1989a). It is readily apparent that this skull shows none of the quantitative criteria found in either early or late metopic synostosis patients. The skull is markedly brachycephalic, with no fronto-orbital narrowing and no compensatory biparietal widening. The provisional estimate of cranial capacity of 1,585 cc, considered in light of the reduced length and near average biparietal width, suggests markedly increased skull height, though no direct data are provided for this feature because the skull base, which is necessary for measuring auricular head height, was removed by researchers in the nineteenth century. The upper face is not increased in length, and the bizygomatic breadth is average. Finally, the interorbital breadth is increased rather than reduced as is the case in every one of our 50 clinical subjects and in other published quantitative studies (Fearon et al., 1996; Posnick et al., 1994). The total morphological pattern is inconsistent with any form of metopic synostosis.

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